WEST

Freeform Search

Database: US Patents Full-Text Database; US Pre-Grant Publication Full-Text Database; JPO Abstracts Database; EPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Term: l3 with L5

Display: 20 **Documents in Display Format:** - **Starting with Number** 1

Generate: ○ Hit List ◉ Hit Count ○ Side by Side ○ Image

Search | Clear | Help | Logout | Interrupt

Main Menu | Show S Numbers | Edit S Numbers | Preferences | Cases

Search History

DATE: Friday, March 21, 2003 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB; PLUR=YES; OP=AND			
L6	l3 with L5	2	L6
L5	lentivir$ near3 vector or hiv-1	8313	L5
L4	lentivir$ near3 vector	648	L4
L3	l1 with L2	409	L3
L2	(parkinson or alzheimer or neural) near3 disease	16248	L2
L1	neurotrophin or gdnf or ngf or fgf or tgf or bmp	12662	L1

END OF SEARCH HISTORY

Generate Collection | Print

Search Results - Record(s) 1 through 2 of 2 returned.

☐ 1. 20020187951 . 08 Nov 01. 12 Dec 02. Lentiviral-mediated growth factor gene therapy for neurodegenerative diseases. Aebischer, Patrick, et al. 514/44; 424/93.2 A61K048/00.

☐ 2. 20020187921 . 04 Apr 02. 12 Dec 02. Transgenic zebrafish models for neurodegenerative disease. Rubeinstein, Amy K.. 514/1; 800/20 800/3 A01K067/027 A61K031/00.

Generate Collection | Print

Terms	Documents
l3 with L5	2

Previous Page Next Page

=> d his

(FILE 'HOME' ENTERED AT 16:24:18 ON 20 MAR 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 16:24:40 ON 20 MAR 2003

L1 50101 S NEUROTROPHIN OR GDNF OR NGF
L2 226592 S (PARKINSON OR ALZHEIMER)(3A)DISEASE
L3 717 S L1(7A)L2
L4 4122 S (LENTIVIR? OR HIV)(3A)VECTOR
L5 23 S L3 AND L4
L6 12 DUP REM L5 (11 DUPLICATES REMOVED)

=> d 1-12 bib ab l6

L6 ANSWER 1 OF 12 MEDLINE DUPLICATE 1
AN 2003105732 IN-PROCESS
DN 22505760 PubMed ID: 12618027
TI Comparative study of GDNF delivery systems for the CNS: polymer rods, encapsulated cells, and **lentiviral vectors**.
AU Bensadoun Jean Charles; Pereira de Almeida Luis; Fine Eric G; Tseng Jack L; Deglon Nicole; Aebischer Patrick
CS Institute of Neurosciences, Swiss Federal Institute of Technology Lausanne EPFL, CH-1015, Lausanne, Switzerland.
SO JOURNAL OF CONTROLLED RELEASE, (2003 Feb 21) 87 (1-3) 107-15.
Journal code: 8607908. ISSN: 0168-3659.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20030306
Last Updated on STN: 20030306
AB Glial cell line-derived neurotrophic factor (**GDNF**) holds great promise for the treatment of **Parkinson's disease**. In humans, its intracerebroventricular administration leads to limiting side effects. Direct parenchymal delivery using mechanical means, or cell and gene therapy represent potential alternatives. In the present study, a representative of each of these three approaches, i.e. polymer rods, genetically modified encapsulated cells and **lentiviral vectors** was analyzed for its ability to release GDNF in the striatum of rats. One week post-surgery, GDNF was detected over a distance of 4 mm with all three methods. At 4 weeks GDNF staining diminished with rods and to a lesser extent with encapsulated cells, whereas it increased with **lentiviral vectors**. Nanogram range of GDNF was measured with all methods at 1 week. At 4 weeks, GDNF levels decreased significantly with rods, whereas they remained stable with encapsulated cells and **lentiviral vectors**. We conclude that all three methods investigated allow striatal delivery of GDNF, but the time during which it needs to be released will determine the approach chosen for clinical application.

L6 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2003 ACS
AN 2002:595345 CAPLUS
DN 137:145613
TI Methods for therapy of neurodegenerative disease of the brain
IN Tuszynski, Mark H.
PA Regents of the University of California, USA
SO U.S. Pat. Appl. Publ., 17 pp., Cont.-in-part of U.S. Ser. No. 620,174.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 4
PATENT NO. KIND DATE APPLICATION NO. DATE

PI	US 2002106350	A1	20020808	US 2001-32952	20011026
	US 6451306	B1	20020917	US 1998-60543	19980415
PRAI	US 1998-60543	A2	19980415		
	US 2000-620174	A2	20000719		

AB A specific clin. protocol is described for use toward therapy of defective, diseased and damaged neurons in the mammalian brain, of particular usefulness for treatment of neurodegenerative conditions such as Parkinson's disease and Alzheimer's disease. The protocol is practiced by delivering a definite concn. of recombinant neurotrophin, such as glial cell-derived neurotrophic factor, into a targeted region of the brain (such as the substantia nigra) using a **lentiviral** expression **vector**. The neurotrophin is delivered to, or within close proximity of, identified defective, diseased or damaged brain cells. The concn. of neurotrophin delivered as part of a neurotrophic compn. varies from 1010 to 1015 neurotrophin encoding viral particles/mL of compn. fluid. Each delivery site receives 2.5-25 .mu.L of neurotrophic compn., delivered slowly, as in over a period of time ranging upwards of 10 min/delivery site. Each delivery site is at, or within 500 .mu.m of, a targeted cell, and no more than about 10 mm from another delivery site. The method stimulates growth of targeted neurons, and reversal of functional deficits assocd. with the neurodegenerative disease being treated.

L6 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2003 ACS
AN 2002:520318 CAPLUS
DN 137:211245
TI Lentivirally delivered glial cell line-derived neurotrophic factor increases the number of striatal dopaminergic neurons in primate models of nigrostriatal degeneration
AU Palfi, Stephane; Leventhal, Liza; Chu, Yaping; Ma, Shuang Y.; Emborg, Marina; Bakay, Roy; Deglon, Nicole; Hantraye, Philippe; Aebischer, Patrick; Kordower, Jeffrey H.
CS Department of Neurological Sciences, Rush-Presbyterian-St. Luke's Medical Center, Chicago, IL, 60612, USA
SO Journal of Neuroscience (2002), 22(12), 4942-4954
CODEN: JNRSDS; ISSN: 0270-6474
PB Society for Neuroscience
DT Journal
LA English
AB The primate striatum contains tyrosine hydroxylase (TH)-immunoreactive (ir) neurons, the nos. of which are augmented after dopamine depletion. Glial cell line-derived neurotrophic factor (GDNF) strongly modulates the viability and phenotypic expression of dopamine ventral mesencephalic neurons. The effect of GDNF on TH-ir neurons intrinsic to the striatum has yet to be investigated. In the present study, stereol. counts of TH-ir striatal neurons in aged and parkinsonian nonhuman primates revealed that GDNF delivered via a **lentiviral vector** (lenti-) further increased the no. of these cells. Aged monkeys treated with lenti-GDNF displayed an 8-fold increase in TH-ir neurons relative to lenti-.beta.-galactosidase-treated monkeys. Unilateral 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine treatment alone in young monkeys resulted in a bilateral 8-fold increase in TH-ir striatal cells. This effect was further magnified 7-fold on the side of lenti-GDNF treatment. These cells colocalized with the neuronal marker neuronal-specific nuclear protein. Some of these cells colocalized with GDNF-ir, indicating that an alteration in phenotype may occur by the direct actions of this trophic factor. Thus, GDNF may mediate plasticity in the dopamine-depleted primate brain, which may serve to compensate for cell loss by converting striatal neurons to a dopaminergic phenotype.
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 2

AN 2002:883080 CAPLUS
TI Neuroprotective for **Parkinson**'s **disease** using viral vector-mediated delivery of **GDNF**
AU McBride, Jodi L.; Kordower, Jeffrey H.
CS Department of Neurological Sciences and Research Center for Brain Repair, Rush University, Chicago, IL, 60612, USA
SO Progress in Brain Research (2002), 138(Plasticity in the Adult Brain: From Genes to Neurotherapy), 421-432
CODEN: PBRRA4; ISSN: 0079-6123
PB Elsevier Science B.V.
DT Journal; General Review
LA English
AB A review on the use of glial cell line-derived neurotrophic factor (GDNF) delivered by viral vectors as a therapeutic strategy for Parkinson's disease (PD). **Lentiviral vectors** contg. gene constructs for GDNF (LV-GDNF) have recently been developed to protect nigrostriatal neurons in various PD models. In addn. to lack of neurotoxicity, LV-GDNF treatment has provided robust pos. effects in numerous preclin. studies, including those employing primate models of PD.
RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2003 ACS
AN 2002:756834 CAPLUS
DN 138:11819
TI Neuroprotection in the rat Parkinson model by intrastriatal GDNF gene transfer using a **lentiviral vector**
AU Georgievska, Biljana; Kirik, Deniz; Rosenblad, Carl; Lundberg, Cecilia; Bjoerklund, Anders
CS Wallenberg Neuroscience Center, Department of Physiological Sciences, Lund University, Lund, 221 84, Swed.
SO NeuroReport (2002), 13(1), 75-82
CODEN: NERPEZ; ISSN: 0959-4965
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB The authors used a recombinant **lentiviral vector** (rLV) for gene delivery of GDNF to the striatum, and assessed its neuroprotective effects in the intrastriatal 6-hydroxydopamine (6-OHDA) lesion model. The level of GDNF expression obtained with the rLV GDNF vector was dose-related and ranged between 0.9-9.3 ng/mg tissue in the transduced striatum, as detd. by ELISA, and 0.2-3.0 ng/mg tissue were detected in the ipsilateral substantia nigra (SN), due to anterograde transport of the GDNF protein. GDNF expression was apparent at 4 days and maintained for .gtoreq.8 mo after injection. Striatal delivery of rLV-GDNF efficiently protected the nigral dopamine (DA) neurons and their projection, against the 6-OHDA lesion (65-77% of intact side). Sprouting of the lesioned axons was obsd. along the nigrostriatal pathway, precisely corresponding to the areas contg. anterogradely transported GDNF.
RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 12 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2001:497475 BIOSIS
DN PREV200100497475
TI Development of a lentiviral regulatable system for GDNF gene delivery.
AU Ridet, J. L. (1); Sommer, B. (1); Spicher, A. (1); Pereira de Almeida, L. (1); Deglon, N. (1); Aebischer, P. (1)
CS (1) Surgical Research and Gene Therapy Center, CHUV, Lausanne Switzerland
SO Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 526. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001
ISSN: 0190-5295.
DT Conference

LA English
SL English
AB In vivo CNS gene therapy approaches require the development of regulated gene expression systems especially for **vectors** such as **lentiviruses** leading to the long-term expression of the transgene. **Lentiviral vectors** carrying the tetracycline (tet)-regulatable system for the controlled expression of green fluorescent protein (d2EGFP) or glial cell line-derived neurotrophic factor (GDNF) were therefore developed. In vitro, we showed that doxycyline (DOX), a tet analogue, decreases d2EGFP expression by 50 to 100 fold in infected 293T cells. **Lentiviral vectors** encoding either for d2EGFP or GDNF were then injected into the striatum of adult rats. DOX (200 microg/ml) was added in the drinking water of defined cohorts. One week later, only scarce GFP-positive cells were detected in the cohort that received DOX treatment whereas numerous neurons with robust GFP expression were observed in the cohort that did not received DOX. The ability to cycle several times the GFP expression as a function of DOX adminsitration was observed in subsequent animals. GDNF expression was also regulated by DOX, although a background revealing a certain level of leakage was observed. We are currently addressing this issue by modifying some characteristics of the tet-regulated system. In parallel, the functional evaluation of **lentiviral vectors** carrying a tet-regulatable cassette for **GDNF** expression is being evaluated in various **Parkinson**'s **disease** models.

L6 ANSWER 7 OF 12 MEDLINE DUPLICATE 3
AN 2001640485 MEDLINE
DN 21548870 PubMed ID: 11690619
TI Sustained delivery of **GDNF**: towards a treatment for **Parkinson**'s **disease**.
AU Zurn A D; Widmer H R; Aebischer P
CS Division of Surgical Research and Gene Therapy Center, Pavillon 4, CHUV, CH-1011, Lausanne, Switzerland.. anne.zurn@chuv.hospvd.ch
SO BRAIN RESEARCH. BRAIN RESEARCH REVIEWS, (2001 Oct) 36 (2-3) 222-9. Ref: 60
Journal code: 8908638. ISSN: 0165-0173.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200202
ED Entered STN: 20011107
Last Updated on STN: 20020209
Entered Medline: 20020208
AB Parkinson's disease (PD) is a neurodegenerative disease characterized by the progressive loss of nigral dopaminergic neurons. Although symptomatic therapies to substitute for the missing neurotransmitter dopamine are efficient at the early stages of the disease, the goal is to find alternative therapies which could protect dopaminergic neurons from the degenerative process. We have used two distinct gene therapy approaches to deliver the neuroprotective molecule glial cell line-derived neurotrophic factor (GDNF) in animal models of the disease: (i) an encapsulated genetically engineered cell line releasing GDNF (ex vivo gene therapy); and (ii) a **lentiviral vector** encoding the GDNF gene (in vivo gene therapy). Both approaches allowed protection of nigral dopaminergic neurons against lesion-induced cell death in rodent as well as monkey models of PD. Behavioral symptoms were also ameliorated in these animals. In addition, co-transplantation of embryonic dopaminergic neuronal grafts and a GDNF-releasing capsule allowed improvement of graft survival and differentiation, thereby accelerating behavioral recovery. These results should lead to clinical application in the near future.

L6 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2003 ACS
AN 2001:146709 CAPLUS
DN 135:282431
TI Gene therapy to the rescue in Parkinson's disease
AU Mandir, A. S.; Dawson, V. L.; Dawson, T. M.
CS Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD, 21287, USA
SO Trends in Pharmacological Sciences (2001), 22(3), 103-105
CODEN: TPHSDY; ISSN: 0165-6147
PB Elsevier Science Ltd.
DT Journal; General Review
LA English
AB A review, with 13 refs., discusses the recent study of Kordower et al., which presents a series of elegant expts. that demonstrate the restorative and protective effects of a glial cell line-derived neurotrophic factor (GDNF), delivered by **lentiviral vectors**, in the brains of both old and parkinsonian primates. Topics discussed include neurotrophic factors as a treatment of **Parkinson**'s **disease**; lentiviral delivery of **GDNF**; and clin. application of lentiviruses.
RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 12 MEDLINE DUPLICATE 4
AN 2000505733 MEDLINE
DN 20508095 PubMed ID: 11052933
TI Neurodegeneration prevented by **lentiviral vector** delivery of **GDNF** in primate models of **Parkinson**'s **disease**.
AU Kordower J H; Emborg M E; Bloch J; Ma S Y; Chu Y; Leventhal L; McBride J; Chen E Y; Palfi S; Roitberg B Z; Brown W D; Holden J E; Pyzalski R; Taylor M D; Carvey P; Ling Z; Trono D; Hantraye P; Deglon N; Aebischer P
CS Department of Neurological Sciences, Rush Presbyterian-St. Luke's Medical Center, Chicago, IL 60612, USA.. jkordowe@rush.edu
NC NS40578 (NINDS)
SO SCIENCE, (2000 Oct 27) 290 (5492) 767-73.
Journal code: 0404511. ISSN: 0036-8075.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200011
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001107
AB Lentiviral delivery of glial cell line-derived neurotrophic factor (lenti-GDNF) was tested for its trophic effects upon degenerating nigrostriatal neurons in nonhuman primate models of **Parkinson**'s **disease** (PD). We injected lenti-**GDNF** into the striatum and substantia nigra of nonlesioned aged rhesus monkeys or young adult rhesus monkeys treated 1 week prior with 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). Extensive GDNF expression with anterograde and retrograde transport was seen in all animals. In aged monkeys, lenti-GDNF augmented dopaminergic function. In MPTP-treated monkeys, lenti-GDNF reversed functional deficits and completely prevented nigrostriatal degeneration. Additionally, lenti-GDNF injections to intact rhesus monkeys revealed long-term gene expression (8 months). In MPTP-treated monkeys, lenti-GDNF treatment reversed motor deficits in a hand-reach task. These data indicate that GDNF delivery using a **lentiviral vector** system can prevent nigrostriatal degeneration and induce regeneration in primate models of PD and might be a viable therapeutic strategy for PD patients.

L6 ANSWER 10 OF 12 SCISEARCH COPYRIGHT 2003 ISI (R)

AN 2002:280139 SCISEARCH
GA The Genuine Article (R) Number: BT94P
TI Gene transfer techniques for the delivery of **GDNF** in **Parkinson**'s **disease**
AU Ridet J L (Reprint); Deglon N; Aebischer P
CS Univ Lausanne, Sch Med, CHUV, Div Surg Res, Pavillon 4, CH-1011 Lausanne, Switzerland (Reprint); Univ Lausanne, Sch Med, CHUV, Div Surg Res, CH-1011 Lausanne, Switzerland; Univ Lausanne, Sch Med, CHUV, Gene Therapy Ctr, CH-1011 Lausanne, Switzerland
CYA Switzerland
SO NEURAL TRANSPLANTATION IN NEURODEGENERATIVE DISEASE: CURRENT STATUS AND NEW DIRECTIONS, (FEB 2000) Vol. 231, pp. 202-215.
Publisher: JOHN WILEY & SONS LTD, BAFFINS LANE, CHICHESTER PO19 1UD, WEST SUSSEX, ENGLAND.
DT Article; Journal
LA English
REC Reference Count: 69
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Parkinson's disease (PD) is a neurodegenerative disorder characterized by motor disturbances caused by an alteration of the dopaminergic nigrostriatal system. Current symptomatic treatments for PD include dopaminergic drug administration, deep brain stimulation, ablative surgery and fetal cell transplantation. Though these approaches have significant beneficial effects, they are hampered by limiting side-effects, but more importantly they do not change the disease progression. Alternative restorative and neuroprotective strategies have therefore to be considered. Neuroprotective effects of neurotrophic factors, anti-apoptotic and antioxidant molecules are currently being investigated for this purpose. Among neurotrophic molecules, the potential of the glial cell line-derived neurotrophic factor (GDNF) to protect the nigral dopaminergic neurons and/or rescue striatal dopamine levels has been extensively documented. For GDNF to become a clinical reality, appropriate delivery techniques will have to be developed. This chapter focuses on the potential of encapsulated cells and viral vectors to locally release neurotrophic factors in experimental models of PD.

L6 ANSWER 11 OF 12 MEDLINE DUPLICATE 5
AN 2000395322 MEDLINE
DN 20341178 PubMed ID: 10877911
TI **Lentiviral vectors** as a gene delivery system in the mouse midbrain: cellular and behavioral improvements in a 6-OHDA model of **Parkinson**'s **disease** using **GDNF**.
AU Bensadoun J C; Deglon N; Tseng J L; Ridet J L; Zurn A D; Aebischer P
CS Division of Surgical Research and Gene Therapy Center, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland.
SO EXPERIMENTAL NEUROLOGY, (2000 Jul) 164 (1) 15-24.
Journal code: 0370712. ISSN: 0014-4886.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200008
ED Entered STN: 20000824
Last Updated on STN: 20001019
Entered Medline: 20000816
AB Local delivery of therapeutic molecules represents one of the limiting factors for the treatment of neurodegenerative disorders. In vivo gene transfer using viral vectors constitutes a powerful strategy to overcome this limitation. The aim of the present study was to validate the **lentiviral vector** as a gene delivery system in the mouse midbrain in the perspective of screening biotherapeutic molecules in mouse models of Parkinson's disease. A preliminary study with a LacZ-encoding vector injected above the substantia nigra of C57BL/6j mice indicated that **lentiviral vectors** can infect approximately 40,000 cells

and diffuse over long distances. Based on these results, glial cell line-derived neurotrophic factor (GDNF) was assessed as a neuroprotective molecule in a 6-hydroxydopamine model of **Parkinson**'s **disease**. **Lentiviral vectors** carrying the cDNA for **GDNF** or mutated GDNF were unilaterally injected above the substantia nigra of C57BL/6j mice. Two weeks later, the animals were lesioned ipsilaterally with 6-hydroxydopamine into the striatum. Apomorphine-induced rotation was significantly decreased in the GDNF-injected group compared to control animals. Moreover, GDNF efficiently protected 69.5% of the tyrosine hydroxylase-positive cells in the substantia nigra against 6-hydroxydopamine-induced toxicity compared to 33.1% with control mutated GDNF. These data indicate that **lentiviral vectors** constitute a powerful gene delivery system for the screening of therapeutic molecules in mouse models of Parkinson's disease.

L6 ANSWER 12 OF 12 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2000:72788 BIOSIS
DN PREV200000072788
TI The **lentiviral vector** as a gene delivery system in the mouse CNS: Cellular and behavioural improvements in a 6-OHDA model of **Parkinson**'s **disease** using **GDNF**.
AU Bensadoun, J. C. (1); Deglon, N. (1); Tseng, J. L. (1); Ridet, J. L. (1); Zurn, A. D. (1); Aebischer, P. (1)
CS (1) Gene Therapy Center and Division of Surgical Research, CHUV, 1011, Lausanne Switzerland
SO Society for Neuroscience Abstracts, (1999) Vol. 25, No. 1-2, pp. 328. Meeting Info.: 29th Annual Meeting of the Society for Neuroscience, Part 1 Miami Beach, Florida, USA October 23-28, 1999 The Society for Neuroscience . ISSN: 0190-5295.
DT Conference
LA English

=>

Experimental Neurology
Volume 164, Issue 1 , July 2000, Pages 15-24

doi:10.1006/exnr.2000.7409 Cite or link using doi

Regular Article

Lentiviral Vectors as a Gene Delivery System in the Mouse Midbrain: Cellular and Behavioral Improvements in a 6-OHDA Model of Parkinson's Disease Using GDNF

Jean-Charles Bensadoun[a], Nicole Déglon[a], Jack L. Tseng[a], Jean-Luc Ridet[a], Anne D. Zurn[a] and Patrick Aebischer[a]

[a] Division of Surgical Research and Gene Therapy Center, Pavillon 4, Centre Hospitalier Universitaire Vaudois, 1011, Lausanne, Switzerland

Received 14 November 1999; accepted 5 January 2000. Available online 26 March 2002.

Abstract

Local delivery of therapeutic molecules represents one of the limiting factors for the treatment of neurodegenerative disorders. *In vivo* gene transfer using viral vectors constitutes a powerful strategy to overcome this limitation. The aim of the present study was to validate the lentiviral vector as a gene delivery system in the mouse midbrain in the perspective of screening biotherapeutic molecules in mouse models of Parkinson's disease. A preliminary study with a LacZ-encoding vector injected above the substantia nigra of C57BL/6j mice indicated that lentiviral vectors can infect approximately 40,000 cells and diffuse over long distances. Based on these results, glial cell line-derived neurotrophic factor (GDNF) was assessed as a neuroprotective molecule in a 6-hydroxydopamine model of Parkinson's disease. Lentiviral vectors carrying the cDNA for GDNF or mutated GDNF were unilaterally injected above the substantia nigra of C57BL/6j mice. Two weeks later, the animals were lesioned ipsilaterally with 6-hydroxydopamine into the striatum. Apomorphine-induced rotation was significantly decreased in the GDNF-injected group compared to control animals. Moreover, GDNF efficiently protected 69.5% of the tyrosine hydroxylase-positive cells in the substantia nigra against 6-hydroxydopamine-induced toxicity compared to 33.1% with control mutated GDNF. These data indicate that lentiviral vectors constitute a powerful

gene delivery system for the screening of therapeutic molecules in mouse models of Parkinson's disease.

Author Keywords: lentivirus; mouse; midbrain; Parkinson's disease; GDNF; animal model

Experimental Neurology
Volume 164, Issue 1 , July 2000 , Pages 15-24

This Document
- **Abstract**
- Abstract + References
- PDF (554 K)

Actions
- E-mail Article

Home | Journals | Abstract Databases | Reference Works | My Alerts | My Profile | Help

Send feedback to ScienceDirect

h c e ce ec c c e ce b c e c